

*DJ*

--According to another feature, the invention relates to dendritic cells that are  $\alpha v\beta_3^-$ ,  $\alpha v\beta_5^+$ , CCR5 $^-$  and CCR7 $^+$ , i.e. are devoid of  $\alpha v\beta_3^-$  and CCR5 receptors and carry  $\alpha v\beta_5$  and CCR7 receptors.--

*PC*

Page 7, replace the paragraph at line 22 to line 27 with the following paragraph:

--However, it was shown that the maturation of DC induced by TNF- $\alpha$  caused the induction of IL-12 production and a dramatic inhibition of IL-10 synthesis after activation by CD40. Thus mature DC according to the invention are capable of triggering the differentiation of naive T lymphocytes into type 1 T lymphocytes. Furthermore, the addition of PGE2 inhibited IL-10 production, but also IL-12 production by mature DC obtained.--

*AS*

Page 12, replace the paragraph at line 23 to line 26 with the following paragraph:

--The results obtained are reported in Figure 2. These results show that, after 6 h of culture with 4  $\mu$ g/ml of CHX, 60% of the XG-1 myeloma cells exhibited characteristics of early apoptotic cell death, i.e. binding of Annexin-V but non-incorporation of PI.--

*AS*

Page 12, replace the paragraph at line 29 to line 34 with the following paragraph:

*AS*

--The phagocytosis of apoptotic cells represents another mode of entry for antigens and plays a major role in the phenomenon of cross priming. Recently, several phagocytic receptors have been identified on DC obtained in the presence of human sera, and it has been shown that a monocyte conditioned medium (MCM), which leads to irreversible DC maturation, downregulates their expression (6).--

Replace the paragraph beginning page 13, line 34 and ending on page 14, line 1 with the following paragraph:

*AS*

--The operation was repeated with six different donors and the mean fluorescence

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intensity (MFI) was measured. The results obtained are shown in Table IV.--.

Page 15, replace the paragraph at line 14 to line 27 with the following paragraph:

--The immature DC obtained with GM-CSF/IL-4 did not produce p70 IL-12, but did produce very large amounts of IL-10 after triggering by CD40 (Table V). The addition of IFN- $\gamma$  together with stimulation by CD40 caused a 30-fold decrease in the production of IL-10 by immature DC activated by CD40. Induction of the maturation of DC with TNF- $\alpha$  caused a dramatic decrease in the production of IL-10 induced by CD40 (10-fold mean reduction), in association with induction of the expression of IL-12. The addition of IFN- $\gamma$  again inhibited the production of IL-10 by mature DC. This is consistent with previous reports showing that IFN- $\gamma$  could be a co-factor for the production of IL-12 induced by CD40 (29,30). However, for the test sample from the other three patients, IFN- $\gamma$  reduced the production of IL-12 by DC obtained in the presence of GM-CSF/IL-4 and TNF- $\alpha$ . Finally, induction of a totally mature DC with TNF- $\alpha$  and PGE2 caused a reduced production of IL-10 and IL-12 after stimulation by CD40, compared with TNF- $\alpha$  alone.--

Replace the paragraph beginning page 15, line 30 and ending on page 16, line 4 with the following paragraph:

--Non-activated T lymphocytes (HLA DR $^+$ ) were purified from healthy volunteers' peripheral blood by two negative selection cycles using microbeads coated with CD14 and CD19 (Dynal, Oslo, Norway), followed by a cocktail of CD16, CD65 and HLA-DR mAbs (Immunotech) and anti-mouse Ig goat microbeads (Dynal). The purity of the CD3 $^+$  T cells was greater than 97%. Increasing numbers of DC treated with mitomycin (50  $\mu$ g/ml) were added to  $1.5 \times 10^5$  allogenic T cells in 200  $\mu$ l of RPMI, 5% ABS. After 5 days of culture, the

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T cell proliferation was measured by the incorporation of tritiated thymidine (1  $\mu$ Ci/well) over the last 12 hours. The results were expressed as the mean counts per minute (cpm)  $\pm$  standard deviation, determined in sextuplet culture wells.--

Page 24, replace the Table with the following Table:

--Table III

Profile of DC receptors

Culture conditions	Mean % of positive cells (MFI)			
	MR	CD36	$\alpha\beta_3$	$\alpha\beta_5$
XV-HA GM/IL-4	98 (233)	88 (89)	0	87 (43)
XV-HA GM/IL-4/TNF	80 (95)*	37 (47)**	0	68 (32)*
XV-HA GM/IL-4/TNF/PGE2	74 (91)*	25 (33)**	0	58 (36)*

XV-HA = X-VIVO 15 medium, 2% HA

\* p < 0.01 by comparison with cells cultivated with GM/IL-4

\*\* p < 0.05 by comparison with cells cultivated with GM/IL-4--

IN THE CLAIMS

Please cancel all claims presently in the application without prejudice or disclaimer of the subject matter thereof, and insert the following new claims:

--14. (New) A method of obtaining dendritic cells, comprising:

- 1) cultivating for 4 to 6 days, mononuclear cells derived from cytapheresis after mobilization, in a serum-free medium supplemented with human albumin, in the presence of a granulocyte-macrophage colony stimulating factor (GM-CSF) and an interleukin (IL) that blocks differentiation towards the macrophagic pathway;
- 2) adding TNF- $\alpha$  and optionally an inflammatory mediator to the culture medium and